

WE CLAIM:

1. A chimeric fatty body-pro-GRF analog with increased biological potency, of the following general formula:

Al-A2-Asp-Ala-Ile-Phe-Thr-A8-Ser-Tyr-Arg-Lys-
Val-Leu-Al5-Gln-Leu-Al8-Ala-Arg-Lys-Leu-Leu-
A24-Asp-Ile-A27-A28-Arg-A30-R₀

wherein,

A1 is Tyr or His;

A2 is Val or Ala;

A8 is Asn or Ser;

Al5 is Ala or Gly;

A24 is Gln or His;

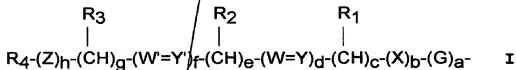
A27 is Met, Ile or Nle;

A28 is Ser or Asp;

A30 is any amino acid sequence of 1 to 15 residues;

R₀ is NH₂;

wherein Al is N- or O-anchored by a hydrophobic tail of the following general formula I:



wherein,

G is a carbonyl, a phosphonyl, a sulfonyl or a sulfinyl group;

X is a oxygen atom, sulfur atom or an amino group (NH);

(W=Y) represents cis or trans (CH=CR₅);

(W'=Y') represents cis or trans (CH=CR₆);

Z is an oxygen or a sulfur atom;

Sub.C1

R₁, R₂ and R₃, independently, are selected from a hydroxyl group, a hydrogen atom, and a linear or branched C₁-C₆ alkyl group;

R₄ is an hydroxyl group, a hydrogen atom or a linear or branched C₅-C₉ alkyl group;

R₅ and R₆, independently, are a hydrogen atom or a linear or branched C₁-C₄ alkyl group;

a is 0 or 1;

b is 0 or 1;

c is 0 to 8;

d is 0 or 1;

e is 0 to 8;

f is 0 or 1;

g is 0 to 8;

h is 0 to 1;

wherein the sum of a, b, c, d, e, f, g and h is such that the hydrophobic tail of formula I has a linear main chain of between 5 and 8 atoms (C, O and/or S).

2. The chimeric fatty body-pro-GRF analog of claim 1, wherein A1 is Tyr or His N-alpha anchored by hydrophobic tail of formula I, wherein both a and b = 1; each of d, f and h = 0; G = carbonyl; X = oxygen atom; R₁, R₂, R₃, R₄ = hydrogen atom and the sum c + e + g = 3, 4, 5 or 6.

3. The chimeric fatty body-pro-GRF analog of claim 1, wherein A1 is Tyr or His N-alpha anchored by hydrophobic tail of formula I, wherein a = 1; each of b, d, f and h = 0; G = carbonyl; R₁, R₂, R₃ and R₄ = hydroxyl group and the sum c + e + g = 4, 5, 6 or 7.

4. The chimeric fatty body-pro-GRF analog of claim 1, wherein A1 is Tyr or His N-alpha anchored by hydrophobic tail of formula I, wherein a = 1; each of b and

B
h= 0; the sum d + f= 1; G= carbonyl; R₁, R₂, R₃ and R₄= hydrogen atom and the sum c + e + g= 2, 3, 4 or 5.

Sub. C2
5. The chimeric fatty body-pro-GRF analog of claim 4, wherein c is 0.

6. The chimeric fatty body-pro-GRF analog of claim 5, wherein A30 is Gln-Gln-Gly-Glu-Ser-Asn-Gln-Glu-Arg-Gly-Ala-Arg-Ala-Arg-Leu.

7. The chimeric fatty body-pro-GRF analog of claim 6, wherein R₀ is NH₂.

8. / The chimeric fatty body-pro-GRF analog of claim 27, of the formula *cis*CH₃-CH₂-CH=CH-CH₂-CO-Tyr-Ala-Asp-Ala-Ile-Phe-Thr-Asn-Ser-Tyr-Arg-Lys-Val-Leu-Gly-Gln-Leu-Ser-Ala-Arg-Lys-Leu-Leu-Gln-Asp-Ile-Met-Ser-Arg-Gln-Gln-Gly-Glu-Ser-Asn-Gln-Glu-Arg-Gly-Ala-Arg-Ala-Arg-Leu-NH₂ or *trans*CH₃-CH₂-CH=CH-CH₂-CO-Tyr-Ala-Asp-Ala-Ile-Phe-Thr-Asn-Ser-Tyr-Arg-Lys-Val-Leu-Gly-Gln-Leu-Ser-Ala-Arg-Lys-Leu-Leu-Gln-Asp-Ile-Met-Ser-Arg-Gln-Gln-Gly-Glu-Ser-Asn-Gln-Glu-Arg-Gly-Ala-Arg-Ala-Arg-Leu-NH₂.

9. The chimeric fatty body-pro-GRF analog of claim 1, wherein A1 is Tyr or His N-alpha anchored by hydrophobic tail of formula I, wherein a= 1; each of b and h= 0; the sum d + f= 2; G= carbonyl; R₁, R₂, R₃ and R₄= hydrogen atom and the sum c + e + g= 0, 1, 2 or 3.

10. The chimeric fatty body-pro-GRF analog of claim 1, wherein A1 is Tyr or His N-alpha anchored by hydrophobic tail of formula I, wherein a= 1; each of b, h, d and f= 0; G= carbonyl; R₁, R₂, R₃ and R₄= hydrogen atom; and the sum c + e + g= 4, 5, 6 or 7.

Sub. C2

11. A pharmaceutical formulation for inducing growth hormone release which comprises as an active ingredient a GRF analog as claimed in claim 1, in association with a pharmaceutically acceptable carrier, excipient or diluent.

12. A method of increasing the level of growth hormone in a patient which comprises administering to said patient an effective amount of a GRF analog as claimed in claim 1.

13. A method for the diagnosis of growth hormone deficiencies in patients, which comprises administering to said patient a GRF analog as claimed in claim 1 and measuring the growth hormone response.

14. A method for the treatment of pituitary dwarfism or growth retardation in a patient, which comprises administering to said patient an effective amount of a GRF analog as claimed in claim 1.

15. A method for the treatment of wound or bone healing in a patient, which comprises administering to said patient an effective amount of a GRF analog as claimed in claim 1.

16. A method for the treatment of osteoporosis in a patient, which comprises administering to said patient an effective amount of a GRF analog as claimed in claim 1.

17. A method for improving protein anabolism in human or animal, which comprises administering to said

Sub. C 2
human or animal an effective amount of a GRF analog as claimed in claim 1.

18. A method for inducing a lipolytic effect in human or animal inflicted with clinical obesity, which comprises administering to said human or animal an effective amount of a GRF analog as claimed in claim 1.

19. A method for the overall upgrading of somatroph function in human or animal, which comprises administering to said human or animal an effective amount of a GRF analog as claimed in claim 1.

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